

WHAT IS CLAIMED IS:

1. A method for conjugating a peptide immunogen via a reactive group of an amino acid residue of the peptide immunogen to a protein/polypeptide carrier having one or more functional groups, the method comprising the steps of:

(a) derivatizing one or more of the functional groups of the protein/polypeptide carrier or optionally to a polypeptide linker attached to the protein/polypeptide carrier to generate a derivatized carrier with reactive sites;

(b) reacting the derivatized protein/polypeptide carrier of step (a) with a reactive group of an amino acid of the peptide immunogen under reaction conditions such that the peptide immunogen is conjugated to the derivatized protein/polypeptide carrier via the functional groups; and

(c) further reacting the conjugate with a capping reagent to inactive free, reactive unreacted functional groups on the derivatized protein/polypeptide carrier, thereby preserving the functionality of the carrier, such that it retains its ability to elicit the desired immune responses against the peptide immunogen that would otherwise not occur without a carrier.

2. The method of claim 1, wherein the carrier is selected from the group consisting of human serum albumin, keyhole limpet hemocyanin (KLH), immunoglobulin molecules, thyroglobulin, ovalbumin, influenza hemagglutinin, PADRE polypeptide, malaria circumsporozoite (CS) protein, hepatitis B surface antigen (HBsAg<sub>19-28</sub>), Heat Shock Protein (HSP) 65, *Mycobacterium tuberculosis*, cholera toxin, cholera toxin mutants with reduced toxicity, diphtheria toxin, CRM<sub>197</sub> protein that is cross-reactive with diphtheria toxin, recombinant Streptococcal C5a peptidase, *Streptococcus pyogenes* ORF1224, *Streptococcus pyogenes* ORF1664, *Streptococcus pyogenes* ORF2452, *Chlamydia pneumoniae* ORF T367, *Chlamydia pneumoniae* ORF T858, Tetanus toxoid, HIV gp120 T1, components recognizing microbial surface adhesive matrix molecules (MSCRAMMS), growth factors, hormones, cytokines and chemokines.

3. The method according to claim 1, wherein the carrier contains a T-cell epitope.

4. The method according to claim 3, wherein the carrier is a bacterial toxoid.

5. The method according to claim 3, wherein the carrier is influenza hemagglutinin.
6. The method according to claim 3, wherein the carrier is the PADRE polypeptide.
7. The method according to claim 3, wherein the carrier is malaria circumsporozite (CS) protein.
8. The method according to claim 3, wherein the carrier is Hepatitis B surface antigen (HBsAg<sub>19-28</sub>).
9. The method according to claim 3, wherein the carrier is heat shock protein 65 (HSP 65).
10. The method according to claim 3, wherein the carrier is a polypeptide from *Mycobacterium tuberculosis* (BCG).
11. The method according to claim 4, wherein the carrier is tetanus toxoid.
12. The method according to claim 4, wherein the bacterial toxoid is CRM 197.
13. The method according to claim 3, wherein the carrier is recombinant Streptococcal C5a peptidase.
14. The method according to claim 3, wherein the carrier is *Streptococcus pyogenes* ORF 1224.
15. The method according to claim 3, wherein the carrier is *Streptococcus pyogenes* ORF 1664.
16. The method according to claim 3, wherein the carrier is *Streptococcus pyogenes* ORF 2452.
17. The method according to claim 3, wherein the carrier is *Chlamydia pneumoniae* ORF T367.

18. The method according to claim 3, wherein the carrier is *Chlamydia pneumoniae* ORF T858.

19. The method according to claim 1, wherein the carrier is a growth factor or hormone, which stimulates or enhances immune response.

20. The method according to claim 19, wherein the growth factor or hormone is selected from the group consisting of IL-1, IL-2,  $\gamma$ -interferon, IL-10, GM-CSF, MIP-1 $\alpha$ , MIP-1 $\beta$ , and RANTES.

21. The method according to claim 1, wherein the peptide immunogen is selected from the group consisting of a bacterial protein, a viral protein, and a eukaryotic protein.

22. The method according to claim 21, wherein the peptide immunogen is derived from a protein antigen from a bacterium.

23. The method according to claim 22, wherein the bacterium is selected from the group consisting of *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Neisseria meningitidis*, *Neisseria gonorrhoeae*, *Haemophilus influenzae*, *Escherichia coli*, *Klebsiella pneumoniae*, *Listeria monocytogenes*, *Vibrio cholerae*, *Clostridium perfringens*, *Clostridium botulinum*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Borrelia burgdorferi*, *Shigella flexneri*, *Shigella boydii*, *Shigella dysenteriae*, *Alloicoccus otitidis* and Group B streptococci.

24. The method according to claim 21, wherein the peptide immunogen is derived from a protein antigen from a virus.

25. The method according to claim 24, wherein the virus is selected from the group consisting of human immunodeficiency virus (HIV), herpes simplex virus (HSV), human papilloma virus (HPV), parainfluenza virus (PIV), vesicular stomatitis virus (VSV), respiratory syncytial virus (RSV), Epstein-Barr virus (EBV), coronavirus, vaccinia virus, rotavirus, rabies virus, hepatitis C virus (HCV) and hepatitis B virus (HBV).

26. The method according to claim 21, wherein the peptide immunogen is derived from a protein antigen from a fungus.

27. The method according to claim 26 wherein the fungus is selected from the group consisting of *Candida albicans*, *Cryptococcus neoformans*, *Coccidioides* species, *Histoplasma* species, and *Aspergillus* species.

28. The method according to claim 21, wherein the peptide immunogen is derived from a protein antigen from a parasite.

29. The method according to claim 28, wherein the parasite is selected from the group consisting of a Plasmodium, a Trypanosome, a Schistosoma, and a Leishmania.

30. The method according to claim 21, wherein the peptide immunogen is derived from a protein antigen from a eukaryote.

31. The method according to claim 30, wherein the eukaryote is a human.

32. The method according to claim 31, wherein the peptide immunogen from the human is derived from a malignant tumor.

33. The method according to claim 32, wherein the tumor antigen is selected from the group consisting of a renal cell carcinoma antigen, a breast carcinoma antigen, a carcinoembryonic antigen, a melanoma (MAGE) antigen, and a prostate cancer specific antigen.

34. The method according to claim 31, wherein the peptide immunogen is from a human A $\beta$  polypeptide.

35. The method according to claim 34, wherein the peptide immunogen is derived from the N-terminal region of A $\beta$  polypeptide.

36. The method according to claim 34, wherein the peptide immunogen is derived from the C-terminal region of A $\beta$  polypeptide.

37. The method according to claim 34, wherein the peptide immunogen is derived from the internal region of A $\beta$  polypeptide.

38. The method according to claim 35, wherein the A $\beta$  peptide immunogen is a fragment of A $\beta$  selected from the group consisting of A $\beta$ 1-5, 1-6, 1-7, 1-10, 1-12, 3-7, 1-3, and 1-4.

39. The method according to claim 34, wherein the A $\beta$  peptide immunogen is a fragment of A $\beta$  selected from the group consisting of A $\beta$  7-11, 3-28, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 17-28, 1-28, 25-35, 35-40 and 35-42.

40. The method according to claim 34, wherein one or more fragments of A $\beta$  peptide immunogen are fused to another peptide immunogen.

41. The method according to claim 40, wherein one molecule of an A $\beta$  peptide immunogen is fused at its C-terminus to the N-terminus of a molecule of the same A $\beta$  peptide immunogen.

42. The method according to claim 40, wherein one molecule of an A $\beta$  peptide immunogen is fused at its C-terminus to the C-terminus of another molecule of the same A $\beta$  peptide immunogen.

43. The method according to claim 40, wherein one molecule of an A $\beta$  peptide immunogen is fused at its C-terminus to the C-terminus of a different molecule of an A $\beta$  peptide immunogen.

44. The method according to claim 40, wherein one molecule of an A $\beta$  peptide immunogen, is fused at its N-terminus to the C-terminus of a molecule of a different A $\beta$  peptide immunogen.

45. The method according to claim 41, 42, 43 or 44, wherein the A $\beta$  peptide immunogen is derived from the N-terminal region of A $\beta$  polypeptide, and is selected from the group consisting of A $\beta$ 1-5, 1-6, 1-7, 1-10, 1-12, 3-7, 1-3, and 1-4.

46. The method according to claim 41, 42, 43 or 44, wherein the A $\beta$  peptide immunogen is a fragment of A $\beta$  selected from the group consisting of A $\beta$  7-11, 3-28, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 17-28, 1-28, 25-35, 35-40 and 35-42.

47. The method according to claim 40, wherein one or more molecules of an A $\beta$  peptide immunogen are linked to one or more molecules of a heterologous peptide.

48. The method according to claim 47, wherein the A $\beta$  peptide immunogen is derived from the N-terminal region of A $\beta$  polypeptide, and is selected from the group consisting of A $\beta$ 1-5, 1-6, 1-7, 1-10, 1-12, 3-7, 1-3, and 1-4.

49. The method according to claim 47, wherein the A $\beta$  peptide immunogen is a fragment of A $\beta$  selected from the group consisting of A $\beta$  7-11, 3-28, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 17-28, 1-28, 25-35, 35-40 and 35-42.

50. The method according to claim 47, wherein the heterologous peptide is selected from the group consisting of a T-cell epitope, a B-cell epitope and combinations thereof.

51. The method according to claim 40, wherein one or more molecules of an A $\beta$  peptide immunogen are linked together in a multiple antigenic peptide (MAP) configuration.

52. The method according to claim 40, wherein one or more molecules of an A $\beta$  peptide immunogen are linked together with one or more molecules of a different A $\beta$  peptide immunogen in a multiple antigenic peptide (MAP) configuration.

53. The method according to claim 51 or 52, wherein the A $\beta$  peptide immunogen is derived from the N-terminal region of A $\beta$  polypeptide, and is selected from the group consisting of A $\beta$ 1-5, 1-6, 1-7, 1-10, 1-12, 3-7, 1-3, and 1-4.

54. The method according to claim 51 or 52, wherein the A $\beta$  peptide immunogen is a fragment of A $\beta$  selected from the group consisting of A $\beta$  7-11, 3-28, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 17-28, 1-28, 25-35, 35-40 and 35-42.

55. The method according to claim 1, wherein the functional group of one or more amino acid molecules of the protein/polypeptide carrier or of the optionally attached polypeptide linker is derivatized using a cross-linking reagent.

56. The method of claim 55, wherein the derivatizing reagent is a zero-length cross-linking reagent.

57. The method of claim 55, wherein the derivatizing reagent is a homobifunctional cross-linking reagent.

58. The method of claim 55, wherein the derivatizing reagent is a heterobifunctional cross-linking reagent.

59. The method of claim 55, wherein the protein/polypeptide carrier is reacted with a haloacetylating agent.

60. The method of claim 58, wherein the heterobifunctional reagent is a reagent which reacts with a primary or an  $\epsilon$ -amine functional group of one or more amino acid residues of the protein/polypeptide carrier and a pendant thiol group of one or more amino acid residues of the peptide immunogen.

61. The method of claim 60, wherein the heterobifunctional reagent is selected from the group consisting of N-succinimidyl bromoacetate, N-succinimidyl-3-(2-pyridyl-thio) propionate (SPDP), and succinimidyl 4-(N-maleimidomethyl) cyclohexane-1-carboxylate (SMCC).

62. The method of claim 61, wherein the primary or  $\epsilon$ -amine functional group is lysine.

63. The method according to claim 60, wherein the pendant thiol group is a cysteine residue of the peptide immunogen.

64. The method according to claim 63, wherein the cysteine residue is localized at the amino-terminus of the peptide immunogen.

65. The method according to claim 63, wherein the cysteine residue is localized at carboxy-terminus of the peptide immunogen.

66. The method according to claim 63, wherein the cysteine residue is localized internally in the peptide immunogen.

67. The method according to claim 63, wherein the pendant thiol group is generated by a thiolating reagent.

68. The method according to claim 67, wherein the thiolating reagent is N-acetyl homocysteinethio lactone.

69. The method according to claim 1, wherein the capping reagent that is used to inactivate free reactive, functional groups on the activated protein/polypeptide carrier is selected from the reagent group consisting of cysteamine, *N*-acetylcysteamine, and ethanolamine.

70. The method according to claim 1, wherein the capping reagent that is used to inactivate free reactive, functional groups on the activated protein/polypeptide carrier is selected from the reagent group consisting of sodium hydroxide, sodium carbonate, ammonium bicarbonate and ammonia.

71. The method of claim 1, wherein the reactive group of the amino acid residue of the peptide immunogen is a free sulfhydryl group.

72. The method of claim 1, wherein one or more of the functional groups are on a linker, which is optionally attached to the protein/polypeptide carrier.

73. The method of claim 72, wherein the linker is a peptide linker.

74. The method of claim 73, wherein the peptide linker is polylysine.

75. A method for conjugating a peptide immunogen to a protein/polypeptide carrier having the structure:



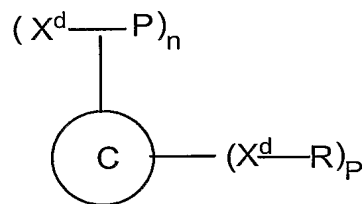
wherein,

C is a protein/polypeptide carrier and X is a derivatizable functional group of an amino acid residue of the protein/polypeptide carrier or optionally of an amino



acid residue of a peptide linker covalently attached to the protein/polypeptide carrier, and wherein  $m$  is an integer greater than 0, but less than or equal to 85, the method comprising the steps of:

- (a) derivatizing one or more of the functional groups of the protein/polypeptide carrier or of the optionally attached linker molecule to generate a derivatized molecule with reactive sites;
- (b) reacting the derivatized protein/polypeptide carrier of step (a) with a reactive group of an amino acid residue of the peptide immunogen to form a covalently coupled peptide immunogen- protein/polypeptide carrier conjugate; and
- (c) further reacting the said conjugate with a capping reagent to inactivate the free reactive functional groups on the activated protein/polypeptide carrier, such that the capped groups are not free to react with other molecules, thereby preserving the functionality of the carrier, such that it retains its ability to elicit the desired immune responses against the peptide immunogen that would otherwise not occur without a carrier., so as to generate a capped peptide immunogen-protein/polypeptide carrier conjugate having the formula:



wherein,

C is the protein/polypeptide carrier and  $X^d$  is a derivatized functional group of an amino acid residue of the protein/polypeptide carrier or optionally of an amino acid residue of a peptide linker covalently attached to the protein/polypeptide carrier, and, wherein,

P is a peptide immunogen molecule covalently attached to the derivatized functional group of the amino acid residue of the protein carrier or optionally of an amino acid residue of a peptide linker covalently attached to a protein/polypeptide carrier,

R is a capping molecule covalently attached to the derivatized functional group of an amino acid residue of the protein/polypeptide carrier or optionally of an amino acid residue of a peptide linker covalently attached to a protein/polypeptide carrier,

$n$  is an integer greater than 0, but less than or equal to 85, and

$p$  is an integer greater than 0, but less than 85.

76. The method of claim 75, wherein the carrier is selected from a group consisting of serum albumin, keyhole limpet hemocyanin (KLH), immunoglobulin molecules, thyroglobulin, ovalbumin, influenza hemagglutinin, PADRE polypeptide, malaria circumsporozoite (CS) protein, hepatitis B surface antigen (HBsAg<sub>19-28</sub>), Heat Shock Protein (HSP) 65, *Mycobacterium tuberculosis*, cholera toxin, cholera toxin mutants with reduced toxicity, diphtheria toxin, CRM<sub>197</sub> protein that is cross-reactive with diphtheria toxin, recombinant Streptococcal C5a peptidase, *Streptococcus pyogenes* ORF1224, *Streptococcus pyogenes* ORF1664, *Streptococcus pyogenes* ORF2452, *Chlamydia pneumoniae* ORF T367, *Chlamydia pneumoniae* ORF T858, Tetanus toxoid, HIV gp120 T1, components recognizing microbial surface adhesive matrix molecules (MSCRAMMS), growth factors, hormones, cytokines and chemokines.

77. The method according to claim 76, wherein the carrier contains a T-cell epitope.

78. The method according to claim 77, wherein the carrier is a bacterial toxoid.

79. The method according to claim 77, wherein the carrier is influenza hemagglutinin.

80. The method according to claim 77, wherein the carrier is PADRE polypeptide.

81. The method according to claim 77, wherein the carrier is malaria circumsporozoite (CS) protein.

82. The method according to claim 77, wherein the carrier is Hepatitis B surface antigen (HBsAg<sub>19-28</sub>).

83. The method according to claim 77, wherein the carrier is heat shock protein 65 (HSP 65).

84. The method according to claim 77, wherein the carrier is a polypeptide from *Mycobacterium tuberculosis* (BCG).

85. The method according to claim 78, wherein the carrier is tetanus toxoid.
86. The method according to claim 78, wherein the bacterial toxoid is CRM 197.
87. The method according to claim 77, wherein the carrier is Streptococcal rC5a peptidase.
88. The method according to claim 77, wherein the carrier is *Streptococcus pyogenes* ORF1224.
89. The method according to claim 77, wherein the carrier is *Streptococcus pyogenes* ORF1664.
90. The method according to claim 77, wherein the carrier is *Streptococcus pyogenes* ORF2452.
91. The method according to claim 77, wherein the carrier is *Chlamydia pneumoniae* ORF T367.
92. The method according to claim 77, wherein the carrier is *Chlamydia pneumoniae* ORF T858.
93. The method according to claim 75, wherein the carrier is a growth factor or hormone, which stimulates or enhances immune response.
94. The method according to claim 93, wherein the growth factor or hormone is selected from a group consisting of IL-1, IL-2,  $\gamma$ -interferon, IL-10, GM-CSF, MIP-1 $\alpha$ , MIP-1 $\beta$ , and RANTES.
95. The method according to claim 75, wherein the peptide immunogen is selected from a bacterial protein, a viral protein, and a eukaryotic protein.
96. The method according to claim 95, wherein the peptide immunogen is derived from a protein antigen from a bacterium.

97. The method according to claim 96, wherein the bacterium is selected from the group consisting of *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Neisseria meningitidis*, *Neisseria gonorrhoeae*, *Haemophilus influenzae*, *Escherichia coli*, *Klebsiella enterobacter*, *Listeria monocytogenes*, *Vibrio cholerae*, *Clostridium perfringens*, *Clostridium botulinum*, *Pseudomonas* species, *Salmonella typhimurium*, *Borrelia burgdorferi*, *Shigella flexneri*, *Shigella boydii*, *Shigella dysenteriae*, *Alloiococcus otitidis* and Group B streptococci.

98. The method according to claim 96, wherein the peptide immunogen is derived from a protein antigen from a virus.

99. The method according to claim 98, wherein the virus is selected from the group consisting of human immunodeficiency virus (HIV), herpes simplex virus (HSV), human papilloma virus (HPV), parainfluenza virus (PIV), vesicular stomatitis virus (VSV), respiratory syncytial virus (RSV), Epstein-Barr virus (EBV), coronavirus, vaccinia virus, rotavirus, rabies virus, hepatitis C virus (HCV) and hepatitis B virus (HBV).

100. The method according to claim 96, wherein the peptide immunogen is derived from a protein antigen from a fungus.

101. The method according to claim 100 wherein the fungus is selected from the group consisting of *Candida albicans*, *Cryptococcus neoformans*, *Coccidioides*, *Histoplasma*, and *Aspergillus*.

102. The method according to claim 96, wherein the peptide immunogen is derived from a protein antigen from a parasite.

103. The method according to claim 102, wherein the parasite is selected from the group consisting of *Plasmodium*, a Trypanosome, a Schistosome, and a Leishmania.

104. The method according to claim 96, wherein the peptide immunogen is derived from a protein antigen from a eukaryote.

105. The method according to claim 104, wherein the eukaryote is a human.

106. The method according to claim 105, wherein peptide immunogen from a human is derived from a malignant tumor.

107. The method according to claim 106, wherein the tumor antigen is a renal cell carcinoma antigen, a breast carcinoma antigen, a carcinoembryonic antigen, a melanoma (MAGE) antigen, and a prostate cancer specific antigen.

108. The method according to claim 105, wherein the peptide immunogen is from a human A $\beta$  polypeptide.

109. The method according to claim 108, wherein the peptide immunogen is derived from the N-terminal region of A $\beta$  polypeptide.

110. The method according to claim 108, wherein the peptide immunogen is derived from the C-terminal region of A $\beta$  polypeptide.

111. The method according to claim 108, wherein the peptide immunogen is derived from the internal region of A $\beta$  polypeptide.

112. The method according to claim 108, wherein the peptide immunogen is a fragment of A $\beta$  selected from the group consisting of A $\beta$ 1-5, 1-6, 1-7, 1-10, 1-12, 3-7, 1-3, and 1-4.

113. The method according to claim 108, wherein the peptide immunogen is a fragment of A $\beta$  selected from the group consisting of A $\beta$  7-11, 3-28, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 17-28, 1-28, 25-35, 35-40 and 35-42.

114. The method according to claim 108, wherein one or more molecules of an A $\beta$  peptide immunogen are fused to another peptide immunogen.

115. The method according to claim 114, wherein one molecule of an A $\beta$  peptide immunogen is fused at its C-terminus to the N-terminus of a another molecule of the same A $\beta$  peptide immunogen.

116. The method according to claim 114, wherein one molecule of an A $\beta$  peptide immunogen is fused at its C-terminus to the C-terminus of another molecule of the same A $\beta$  peptide immunogen.

117. The method according to claim 114, wherein one molecule of an A $\beta$  peptide immunogen is fused at its C-terminus to the C-terminus of a molecule of a different A $\beta$  peptide immunogen.

118. The method according to claim 114, wherein one molecule of an A $\beta$  peptide immunogen is fused at its N-terminus to the C-terminus of a molecule of a different A $\beta$  peptide immunogen.

119. The method according to claim 115, 116, 117 or 118, wherein the A $\beta$  fragment is derived from the N-terminal region of the A $\beta$  polypeptide, and is selected from the group consisting of A $\beta$ 1-5, 1-6, 1-7, 1-10, 1-12, 3-7, 1-3, and 1-4.

120. The method according to claim 115, 116, 117 or 118, wherein the A $\beta$  fragment is a fragment of A $\beta$  selected from A $\beta$  7-11, 3-28, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 17-28, 1-28, 25-35, 35-40 and 35-42.

121. The method according to claim 114, wherein one or more molecules of an A $\beta$  peptide immunogen are fused to one or more molecules of a heterologous peptide.

122. The method according to claim 121, wherein the A $\beta$  peptide immunogen is derived from the N-terminal region of A $\beta$  polypeptide, and is selected from the group consisting of A $\beta$ 1-5, 1-6, 1-7, 1-10, 1-12, 3-7, 1-3, and 1-4.

123. The method according to claim 121, wherein the A $\beta$  peptide immunogen is a fragment of A $\beta$  selected from the group consisting of A $\beta$  7-11, 3-28, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 17-28, 1-28, 25-35, 35-40 and 35-42.

124. The method according to claim 121, wherein the heterologous peptide is selected from the group consisting of a T-cell epitope, a B-cell epitope and combinations thereof.

125. The method according to claim 114, wherein one or more molecules of an A $\beta$  peptide immunogen are linked together in a multiple antigenic peptide (MAP) configuration.

126. The method according to claim 114, wherein one or more molecules of an A $\beta$  peptide immunogen are linked together with one or more molecules of a different A $\beta$  peptide immunogen in a multiple antigenic peptide (MAP) configuration.

127. The method according to claim 125 or 126, wherein the A $\beta$  peptide immunogen is derived from the N-terminal region of A $\beta$  polypeptide, and is selected from the group consisting of A $\beta$ 1-5, 1-6, 1-7, 1-10, 1-12, 3-7, 1-3, and 1-4.

128. The method according to claim 125 or 126, wherein the A $\beta$  peptide immunogen is a fragment of A $\beta$  selected from the group consisting of A $\beta$  7-11, 3-28, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 17-28, 1-28, 25-35, 35-40 and 35-42.

129. The method according to claim 75, wherein the functional group of one or more amino acid molecules of the protein/polypeptide carrier or of the optionally attached polypeptide linker is derivatized using a cross-linking reagent.

130. The method of claim 129, wherein the derivatizing reagent is a zero-length cross-linking reagent.

131. The method of claim 129, wherein the derivatizing reagent is a homobifunctional cross-linking reagent.

132. The method of claim 129, wherein the derivatizing reagent is a heterobifunctional cross-linking reagent.

133. The method of claim 129, wherein the protein/polypeptide carrier is reacted with a haloacetylating agent.

134. The method of claim 133, wherein the heterobifunctional reagent is a reagent which reacts with a primary or an  $\epsilon$ -amine functional group of one or more amino acid residues of the protein/polypeptide carrier and a pendant thiol group of one or more amino acid residues of the peptide immunogen.

135. The method of claim 134, wherein the heterobifunctional reagent is N-succinimidyl bromoacetate, N-succinimidyl-3-(2-pyridyl-thio) propionate (SPDP), and succinimidyl 4-(N-maleimidomethyl) cyclohexane-1-carboxylate (SMCC).

136. The method of claim 134, wherein the primary or  $\epsilon$ -amine functional group is lysine.

137. The method according to claim 136, wherein derivatization of the primary or  $\epsilon$ -amine functional group of the amino acid residue lysine of the protein/polypeptide carrier with N-succinimidyl bromo acetate results in the bromoacetylation of the primary or  $\epsilon$ -amine residues on lysine residues on the protein/polypeptide carrier.

138. The method according to claim 134, wherein the pendant thiol group is a cysteine residue of the peptide immunogen.

139. The method according to claim 138, wherein the cysteine residue is localized at the amino-terminus of the peptide immunogen.

140. The method according to claim 138, wherein the cysteine residue is localized at carboxy-terminus of the peptide immunogen.

141. The method according to claim 138, wherein the cysteine residue is localized internally in the peptide immunogen.

142. The method according to claim 138, wherein the pendant thiol group is generated by a thiolating reagent.

143. The method according to claim 142, wherein the thiolating reagent is N-acetyl homocysteinethio lactone.

144. The method according to claim 75, wherein the capping reagent that is used to inactivate free reactive, functional groups of the activated protein/polypeptide carrier is selected from the reagent group consisting of cysteamine, N-acetylcysteamine, and ethanolamine.

145. The method according to claim 75, wherein the capping reagent that is used to inactivate free reactive, functional groups on the activated protein/polypeptide carrier is selected from the reagent group consisting of sodium hydroxide, sodium carbonate, ammonium bicarbonate and ammonia.



146. The method of claim 75, wherein the reactive group of the amino acid residue of the peptide immunogen is a free sulfhydryl group.

147. The method of claim 75, wherein one or more of the functional groups are on a linker optionally attached to the protein/polypeptide carrier.

148. The method of claim 147, wherein the linker is a peptide linker.

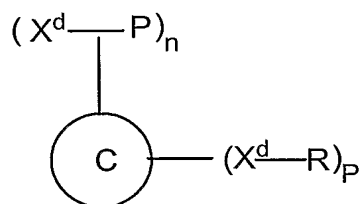
149. The method of claim 148, wherein the peptide linker is polylysine.

150. A peptide immunogen-protein/polypeptide carrier conjugate wherein the protein/polypeptide carrier has the formula:



wherein,

C is a protein/polypeptide carrier and X is a derivatizable functional group of an amino acid residue on the protein/polypeptide carrier or optionally of an amino acid residue of a peptide linker covalently attached to the protein/polypeptide carrier, and, wherein m is an integer greater than 0, but less than or equal to 85, and wherein the peptide immunogen-protein/polypeptide carrier conjugate has the formula:



wherein,

C is the protein/polypeptide carrier and  $X^d$  is a derivatized functional group of an amino acid residue of the protein/polypeptide carrier or optionally of an amino acid residue of a peptide linker covalently attached to the protein/polypeptide carrier, and, wherein, P is a peptide immunogen molecule covalently attached to the derivatized functional group of the amino acid residue of the protein carrier or optionally of an amino acid residue

of a peptide linker covalently attached to a protein/polypeptide carrier, R is a capping molecule covalently attached to the derivatized functional group of an amino acid residue of the protein/polypeptide carrier or optionally of an amino acid residue of a peptide linker covalently attached to a protein/polypeptide carrier, thereby preserving the functionality of the carrier such that it retains its ability to elicit the desired immune responses against the peptide immunogen that would otherwise not occur without a carrier., n is an integer greater than 0, but less than or equal to 85, and p is an integer greater than 0, but less than 85.

151. The conjugate according to claim 150, wherein the carrier is selected from a group consisting of serum albumin, keyhole limpet hemocyanin (KLH), immunoglobulin molecules, thyroglobulin, ovalbumin, influenza hemagglutinin, PADRE polypeptide, malaria circumsporozite (CS) protein, hepatitis B surface antigen (HBsAg<sub>19-28</sub>), Heat Shock Protein (HSP) 65, *Mycobacterium tuberculosis*, cholera toxin, cholera toxin mutants with reduced toxicity, diphtheria toxin, CRM<sub>197</sub> protein that is cross-reactive with diphtheria toxin, recombinant Streptococcal C5a peptidase, *Streptococcus pyogenes* ORF1224, *Streptococcus pyogenes* ORF1664, *Streptococcus pyogenes* ORF2452, *Chlamydia pneumoniae* ORF T367, *Chlamydia pneumoniae* ORF T858, Tetanus toxoid, HIV gp120 T1, components recognizing microbial surface adhesive matrix molecules (MSCRAMMS), growth factors, hormones, cytokines and chemokines.

152. The conjugate according to claim 150, wherein the carrier contains a T-cell epitope.

153. The conjugate according to claim 152, wherein the carrier is a bacterial toxoid.

154. The conjugate according to claim 152, wherein the carrier is influenza hemagglutinin.

155. The conjugate according to claim 152, wherein the carrier is PADRE polypeptide.

156. The conjugate according to claim 152, wherein the carrier is malaria circumsporozite (CS) protein.

157. The conjugate according to claim 152, wherein the carrier is Hepatitis B surface antigen (HBsAg<sub>19-28</sub>).

158. The conjugate according to claim 152, wherein the carrier is heat shock protein 65 (HSP 65).

159. The conjugate according to claim 152, wherein the carrier is a polypeptide from *Mycobacterium tuberculosis* (BCG).

160. The conjugate according to claim 153, wherein the carrier is tetanus toxoid.

161. The conjugate according to claim 153, wherein the bacterial toxoid is CRM<sub>197</sub>.

162. The conjugate according to claim 152, wherein the carrier is Streptococcal rC5a peptidase.

163. The conjugate according to claim 152, wherein the carrier is *Streptococcus pyogenes* ORF1224.

164. The conjugate according to claim 152, wherein the carrier is *Streptococcus pyogenes* ORF1664.

165. The conjugate according to claim 152, wherein the carrier is *Streptococcus pyogenes* ORF2452.

166. The conjugate according to claim 152, wherein the carrier is *Chlamydia pneumoniae* ORF T367.

167. The conjugate according to claim 152, wherein the carrier is *Chlamydia pneumoniae* ORF T858.

168. The conjugate according to claim 150, wherein the carrier is a growth factor or hormone, which stimulates or enhances immune response.

169. The conjugate according to claim 168, wherein the growth factor or hormone is selected from a group consisting of IL-1, IL-2,  $\gamma$ -interferon, IL-10, GM-CSF, MIP-1 $\alpha$ , MIP-1 $\beta$ , and RANTES.

170. The conjugate according to claim 150, wherein the peptide immunogen is selected from the group consisting of a bacterial protein, a viral protein, and a eukaryotic protein.

171. The conjugate according to claim 170, wherein the peptide immunogen is derived from a protein antigen from a bacterium.

172. The conjugate according to claim 171, wherein the bacterium is selected from the group consisting of *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Neisseria meningitidis*, *Neisseria gonorrhoeae*, *Haemophilus influenzae*, *Escherichia coli*, *Klebsiella enterobacter*, *Listeria monocytogenes*, *Vibrio cholerae*, *Clostridium perfringens*, *Clostridium botulinum*, *Pseudomonas* species, *Salmonella typhimurium*, *Borrelia burgdorferi*, *Shigella flexneri*, *Shigella boydii*, *Shigella dysenteriae*, *Alloiococcus otitidis* and Group B streptococci.

173. The conjugate according to claim 170, wherein the peptide immunogen is derived from a protein antigen from a virus.

174. The conjugate according to claim 173, wherein the virus is selected from the group consisting of a human immunodeficiency virus (HIV), a herpes simplex virus (HSV), a human papilloma virus (HPV), a parainfluenza virus (PIV), a vesicular stomatitis virus (VSV), a respiratory syncytial virus (RSV), an Epstein-Barr virus (EBV), a coronavirus, a vaccinia virus, a rotavirus, a rabies virus, a hepatitis C virus (HCV) and a hepatitis B virus (HBV).

175. The conjugate according to claim 170, wherein the peptide immunogen is derived from a protein antigen from a fungus.

176. The conjugate according to claim 175, wherein the fungus is selected from the group consisting of *Candida albicans*, *Cryptococcus neoformans*, *Coccidioides*, *Histoplasma*, and *Aspergillus*.

177. The conjugate according to claim 170, wherein the peptide immunogen is derived from a protein antigen from a parasite.

178. The conjugate according to claim 177, wherein the parasite is selected from the group consisting of a Plasmodium, a Trypanosome, a Schistosoma, and a Leishmania.

179. The conjugate according to claim 170, wherein the peptide immunogen is derived from a protein antigen from an eukaryote.

180. The conjugate according to claim 179, wherein the eukaryote is a human.

181. The conjugate according to claim 180, wherein peptide immunogen from the human is derived from a malignant tumor.

182. The conjugate according to claim 181, wherein the tumor antigen is selected from the group consisting of a renal cell carcinoma antigen, a breast carcinoma antigen, a carcinoembryonic antigen, a melanoma (MAGE) antigens, and prostate specific membrane antigen (PSMA).

183. The conjugate according to claim 180, wherein the peptide immunogen is from a human A $\beta$  polypeptide.

184. The conjugate according to claim 183, wherein the peptide immunogen is derived from the N-terminal region of A $\beta$  polypeptide.

185. The conjugate according to claim 183, wherein the peptide immunogen is derived from the C-terminal region of A $\beta$  polypeptide.

186. The conjugate according to claim 183, wherein the peptide immunogen is derived from the internal region of A $\beta$  polypeptide.

187. The conjugate according to claim 183, wherein the peptide immunogen is a fragment of A $\beta$  selected from the group consisting of A $\beta$ 1-5, 1-6, 1-7, 1-10, 1-12, 3-7, 1-3, and 1-4.

188. The conjugate according to claim 183, wherein the peptide immunogen is a fragment of A $\beta$  selected from the group consisting of A $\beta$  7-11, 3-28, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 17-28, 1-28, 25-35, 35-40 and 35-42.

189. The conjugate according to claim 183, wherein one or more molecules of A $\beta$  are fused to one or more molecules of another peptide immunogen.

190. The conjugate according to claim 189, wherein one molecule of an A $\beta$  peptide immunogen is fused at its C-terminus to the N-terminus of another molecule of the same A $\beta$  peptide immunogen.

191. The conjugate according to claim 189, wherein one molecule of an A $\beta$  peptide immunogen is fused at its C-terminus to the C-terminus of another molecule of the same A $\beta$  peptide immunogen.

192. The conjugate according to claim 189, wherein a molecule of an A $\beta$  peptide immunogen is fused at its C-terminus to the C-terminus of a molecule of a different A $\beta$  peptide immunogen.

193. The conjugate according to claim 189 wherein one molecule of an A $\beta$  peptide immunogen is fused at its N-terminus to the C-terminus of a molecule of a different A $\beta$  peptide immunogen.

194. The conjugate according to claim 190, 191, 192 or 193, wherein the A $\beta$  peptide immunogen is derived from the N-terminal region of the A $\beta$  polypeptide, and is selected from the group consisting of A $\beta$ 1-5, 1-6, 1-7, 1-10, 1-12, 3-7, 1-3, and 1-4.

195. The conjugate according to claim 190, 191, 192 or 193, wherein the A $\beta$  peptide immunogen is a fragment of A $\beta$  selected from the group consisting of A $\beta$  7-11, 3-28, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 17-28, 1-28, 25-35, 35-40 and 35-42.

196. The conjugate according to claim 189, wherein one or more molecules of an A $\beta$  peptide immunogen are linked to one or more molecules of a heterologous peptide.

197. The conjugate according to claim 196, wherein the A $\beta$  peptide immunogen is derived from the N-terminal region of A $\beta$  polypeptide, and is selected from the group consisting of A $\beta$ 1-5, 1-6, 1-7, 1-10, 1-12, 3-7, 1-3, and 1-4.

198. The conjugate according to claim 196, wherein the A $\beta$  fragment is a fragment of A $\beta$  selected from the group consisting of A $\beta$  7-11, 3-28, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 17-28, 1-28, 25-35, 35-40 and 35-42.

199. The conjugate according to claim 196, wherein the heterologous peptide is selected from the group consisting of a T-cell epitope, a B-cell epitope and combinations thereof.

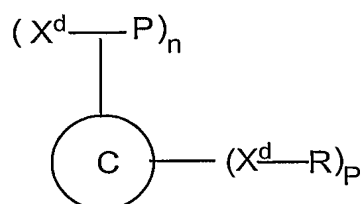
200. The conjugate according to claim 189, wherein one or more molecules of an A $\beta$  peptide immunogen are linked together in a multiple antigenic peptide (MAP) configuration.

201. The conjugate according to claim 189, wherein one or more molecules of an A $\beta$  peptide immunogen are linked with one or more copies of a different A $\beta$  peptide immunogen in a multiple antigenic peptide (MAP) configuration.

202. The conjugate according to claim 200 or 201, wherein the A $\beta$  peptide immunogen is derived from the N-terminal region of A $\beta$  polypeptide, and is selected from the group consisting of A $\beta$ 1-5, 1-6, 1-7, 1-10, 1-12, 3-7, 1-3, and 1-4.

203. The conjugate according to claim 200 or 201, wherein the A $\beta$  peptide immunogen is a fragment of A $\beta$  selected from the group consisting of A $\beta$  7-11, 3-28, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 17-28, 1-28, 25-35, 35-40 and 35-42.

204. A peptide immunogen-protein/polypeptide carrier conjugate generated according to the method of claim 75 and having the formula:



wherein,

C is the protein/polypeptide carrier and  $X^d$  is a derivatized functional group of an amino acid residue of the protein/polypeptide carrier or optionally of an amino acid residue of a peptide linker covalently attached to the protein/polypeptide carrier, and, wherein, P is a peptide immunogen molecule covalently attached to the derivatized functional group of the amino acid residue of the protein carrier or optionally of an amino acid residue of a peptide linker covalently attached to a protein/polypeptide carrier, R is a capping molecule covalently attached to the derivatized functional group of an amino acid residue of the protein/polypeptide carrier or optionally of an amino acid residue of a peptide linker covalently attached to a protein/polypeptide carrier, which preserves the functionality of the carrier, such that it retains its ability to elicit the desired immune responses against the peptide immunogen that would otherwise not occur without a carrier, n is an integer greater than 0, but less than or equal to 85, and p is an integer greater than 0, but less than 85.

205. The conjugate according to claim 204 wherein the carrier is selected from the group consisting of human serum albumin, keyhole limpet hemocyanin (KLH), immunoglobulin molecules, thyroglobulin, ovalbumin, influenza hemagglutinin, PADRE polypeptide, malaria circumsporozoite (CS) protein, hepatitis B surface antigen (HBsAg<sub>19-28</sub>), Heat Shock Protein (HSP) 65, *Mycobacterium tuberculosis*, cholera toxin, cholera toxin mutants with reduced toxicity, diphtheria toxin, CRM<sub>197</sub> protein that is cross-reactive with diphtheria toxin, recombinant Streptococcal C5a peptidase, *Streptococcus pyogenes* ORF1224, *Streptococcus pyogenes* ORF1664, *Streptococcus pyogenes* ORF2452, *Chlamydia pneumoniae* ORF T367, *Chlamydia pneumoniae* ORF T858, Tetanus toxoid, HIV gp120 T1, components recognizing microbial surface adhesive matrix molecules (MSCRAMMS), growth factors, hormones, cytokines and chemokines.

206. The conjugate according to claim 204 wherein the carrier contains a T-cell epitope.

207. The conjugate according to claim 206, wherein the carrier is a bacterial toxoid.

208. The conjugate according to claim 206, wherein the carrier is influenza hemagglutinin.



209. The conjugate according to claim 206, wherein the carrier is PADRE polypeptide.

210. The conjugate according to claim 206, wherein the carrier is malaria circumsporozite (CS) protein.

211. The conjugate according to claim 206, wherein the carrier is Hepatitis B surface antigen (HSBAg<sub>19-28</sub>).

212. The conjugate according to claim 206, wherein the carrier is heat shock protein 65 (HSP 65).

213. The conjugate according to claim 206, wherein the carrier is a polypeptide from *Mycobacterium tuberculosis* (BCG).

214. The conjugate according to claim 207, wherein the carrier is tetanus toxoid.

215. The conjugate according to claim 207, wherein the bacterial toxoid is CRM<sub>197</sub>.

216. The conjugate according to claim 206, wherein the carrier is Streptococcal rC5a peptidase.

217. The conjugate according to claim 206, wherein the carrier is *Streptococcus pyogenes* ORF1224.

218. The conjugate according to claim 206, wherein the carrier is *Streptococcus pyogenes* ORF1664.

219. The conjugate according to claim 206, wherein the carrier is *Streptococcus pyogenes* ORF2452.

220. The conjugate according to claim 206, wherein the carrier is *Chlamydia pneumoniae* ORF T367.

221. The conjugate according to claim 206, wherein the carrier is *Chlamydia pneumoniae* ORF T858.

222. The conjugate according to claim 206, wherein the carrier is a growth factor or hormone, which stimulates or enhances immune response.

223. The conjugate according to claim 222, wherein the growth factor or hormone is selected from a group consisting of IL-1, IL-2,  $\gamma$ -interferon, IL-10, GM-CSF, MIP-1 $\alpha$ , MIP-1 $\beta$ , and RANTES.

224. The conjugate according to claim 206, wherein the peptide immunogen is selected from the group consisting of a bacterial protein, a viral protein, a fungal protein, a parasite protein and a eukaryotic protein.

225. The conjugate according to claim 224, wherein the peptide immunogen is derived from a protein antigen from a bacterium.

226. The conjugate according to claim 225, wherein the bacterium is selected from the group consisting of *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Neisseria meningitidis*, *Neisseria gonorrhoeae*, *Haemophilus influenzae*, *Escherichia coli*, *Klebsiella enterobacter*, *Listeria monocytogenes*, *Vibrio cholerae*, *Clostridium perfringens*, *Clostridium botulinum*, *Pseudomonas* species, *Salmonella typhimurium*, *Borrelia burgdorferi*, *Shigella flexneri*, *Shigella boydii*, *Shigella dysenteriae*, *Alloiococcus otitidis* and Group B streptococci.

227. The conjugate according to claim 224, wherein the peptide immunogen is derived from a protein antigen from a virus.

228. The conjugate according to claim 227, wherein the virus is selected from the group consisting of a human immunodeficiency virus (HIV), a herpes simplex virus (HSV), a human papilloma virus (HPV), a parainfluenza virus (PIV), a vesicular stomatitis virus (VSV), a respiratory syncytial virus (RSV), Epstein-Barr virus (EBV), a coronavirus, a vaccinia virus, rotavirus, a rabies virus, a hepatitis C virus (HCV) and a hepatitis B virus (HBV).

229. The conjugate according to claim 224, wherein the peptide immunogen is derived from a protein antigen from a fungus.

230. The conjugate according to claim 229, wherein the fungus is selected from the group consisting of *Candida albicans*, *Cryptococcus neoformans*, *Coccidioides*, *Histoplasma*, and *Aspergillus*.

231. The conjugate according to claim 224, wherein the peptide immunogen is derived from a protein antigen from a parasite.

232. The conjugate according to claim 231, wherein the parasite is selected from the group consisting of a *Plasmodium*, a *Trypanosome*, a *Schistosoma*, and a *Leishmania*.

233. The conjugate according to claim 224, wherein the peptide immunogen is derived from a protein antigen from an eukaryote.

234. The conjugate according to claim 233, wherein the eukaryote is a human.

235. The conjugate according to claim 234, wherein peptide immunogen from the human is derived from a malignant tumor.

236. The conjugate according to claim 235, wherein the tumor antigen is selected from a renal cell carcinoma antigen, a breast carcinoma antigen, a carcinoembryonic antigen, a melanoma antigen, and a prostate cancer specific antigen.

237. The conjugate according to claim 234, wherein the peptide immunogen is from a human A $\beta$  polypeptide.

238. The conjugate according to claim 237, wherein the peptide immunogen is derived from the N-terminal region of A $\beta$  polypeptide.

239. The conjugate according to claim 237, wherein the peptide immunogen is derived from the C-terminal region of A $\beta$  polypeptide.

240. The conjugate according to claim 237, wherein the peptide immunogen is derived from the internal region of A $\beta$  polypeptide.

241. The conjugate according to claim 237, wherein the A $\beta$  peptide immunogen is a fragment of A $\beta$  selected from the group consisting of A $\beta$ 1-5, 1-6, 1-7, 1-10, 1-12, 3-7, 1-3, and 1-4.

242. The conjugate according to claim 237, wherein the A $\beta$  peptide immunogen is a fragment of A $\beta$  selected from the group consisting of A $\beta$  7-11, 3-28, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 17-28, 1-28, 25-35, 35-40 and 35-42.

243. The conjugate according to claim 237, wherein one or more molecules of an A $\beta$  peptide immunogen are fused to another peptide immunogen.

244. The conjugate according to claim 243, wherein one molecule of an A $\beta$  peptide immunogen is fused at its C-terminus to the N-terminus of another molecule of the same A $\beta$  peptide immunogen.

245. The conjugate according to claim 243, wherein one molecule of an A $\beta$  peptide immunogen is fused at its C-terminus to the C-terminus of another molecule of the same A $\beta$  peptide immunogen.

246. The conjugate according to claim 243, wherein one molecule of an A $\beta$  peptide immunogen is fused at its C-terminus to the C-terminus of a molecule of a different A $\beta$  peptide immunogen.

247. The conjugate according to claim 243 wherein one molecule of an A $\beta$  peptide immunogen is fused at its N-terminus to the C-terminus of a molecule of a different A $\beta$  peptide immunogen.

248. The conjugate according to claim 244, 245, 246 or 247, wherein the A $\beta$  peptide immunogen is derived from the N-terminal region of the A $\beta$  polypeptide, and is selected from the group consisting of A $\beta$ 1-5, 1-6, 1-7, 1-10, 1-12, 3-7, 1-3, and 1-4.

249. The conjugate according to claim 244, 245, 246 or 247, wherein the A $\beta$  peptide immunogen is a fragment of A $\beta$  selected from the group consisting of A $\beta$  7-11, 3-28, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 17-28, 1-28, 25-35, 35-40 and 35-42.

250. The conjugate according to claim 243, wherein one or more fragments of A $\beta$  are linked to one or more molecules of a heterologous peptide.

251. The conjugate according to claim 250, wherein the A $\beta$  peptide immunogen is derived from the N-terminal region of A $\beta$  polypeptide, and is selected from the group consisting of A $\beta$ 1-5, 1-6, 1-7, 1-10, 1-12, 3-7, 1-3, and 1-4.

252. The conjugate according to claim 250, wherein the A $\beta$  peptide immunogen is a fragment of A $\beta$  selected from the group consisting of A $\beta$  7-11, 3-28, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 17-28, 1-28, 25-35, 35-40 and 35-42.

253. The conjugate according to claim 250, wherein the heterologous peptide is selected from the group consisting of a T-cell epitope, a B-cell epitope and combinations thereof.

254. The conjugate according to claim 243, wherein one or more molecules of an A $\beta$  peptide immunogen are linked together in a multiple antigenic peptide (MAP) configuration.

255. The conjugate according to claim 243, wherein one or more molecules of an A $\beta$  peptide immunogen are linked with one or more copies of a different A $\beta$  peptide immunogen in a multiple antigenic peptide (MAP) configuration.

256. The conjugate according to claim 254 or 255, wherein the A $\beta$  peptide immunogen is derived from the N-terminal region of A $\beta$  polypeptide, and is selected from the group consisting of A $\beta$ 1-5, 1-6, 1-7, 1-10, 1-12, 3-7, 1-3, and 1-4.

257. The conjugate according to claim 254 or 255, wherein the A $\beta$  peptide immunogen is a fragment of A $\beta$  selected from the group consisting of A $\beta$  7-11, 3-28, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 17-28, 1-28, 25-35, 35-40 and 35-42.

258. The conjugate according to claim 243, wherein one or more molecules of an A $\beta$  peptide immunogen are linked with one or more molecules of a heterologous peptide.

259. The conjugate according to claim 258, wherein the heterologous peptide is selected from the group consisting of a T-cell epitope, a B-cell epitope and combinations thereof.

260. The conjugate according to claim 258, wherein the A $\beta$  peptide immunogen is derived from the N-terminal region of A $\beta$  polypeptide, and is a fragment of A $\beta$  selected from the group consisting of A $\beta$ 1-5, 1-6, 1-7, 1-10, 1-12, 3-7, 1-3, and 1-4.

261. The conjugate according to claim 258, wherein the A $\beta$  peptide immunogen is a fragment of A $\beta$  selected from the group consisting of A $\beta$  7-11, 3-28, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 17-28, 1-28, 25-35, 35-40 and 35-42.

262. An immunogenic composition, comprising a conjugate of a peptide immunogen with a protein/polypeptide carrier generated by the method of claim 75, together with one or more pharmaceutically acceptable excipients, diluents, and /or adjuvants.

263. The immunogenic composition according to claim 262, wherein the carrier is selected from the group consisting of human serum albumin, keyhole limpet hemocyanin (KLH), immunoglobulin molecules, thyroglobulin, ovalbumin, influenza hemagglutinin, PADRE polypeptide, malaria circumsporozoite (CS) protein, hepatitis B surface antigen (HBsAg<sub>19-28</sub>), Heat Shock Protein (HSP) 65, *Mycobacterium tuberculosis*, cholera toxin, cholera toxin mutants with reduced toxicity, diphtheria toxin, CRM<sub>197</sub> protein that is cross-reactive with diphtheria toxin, recombinant Streptococcal C5a peptidase, *Streptococcus pyogenes* ORF1224, *Streptococcus pyogenes* ORF1664, *Streptococcus pyogenes* ORF2452, *Chlamydia pneumoniae* ORF T367, *Chlamydia pneumoniae* ORF T858, Tetanus toxoid, HIV gp120 T1, components recognizing microbial surface adhesive matrix molecules (MSCRAMMS), growth factors, hormones, cytokines and chemokines.

264. The immunogenic composition according to claim 262, wherein the carrier contains a T-cell epitope.

265. The method according to claim 264 wherein the carrier is a bacterial toxoid.

266. The immunogenic composition according to claim 264, wherein the carrier is influenza hemagglutinin.

267. The immunogenic composition according to claim 264, wherein the carrier is PADRE polypeptide.

268. The immunogenic composition according to claim 264, wherein the carrier is malaria circumsporozite (CS) protein.

269. The immunogenic composition according to claim 264, wherein the carrier is Hepatitis B surface antigen (HSBAg<sub>19-28</sub>).

270. The immunogenic composition according to claim 264, wherein the carrier is heat shock protein 65 (HSP 65).

271. The immunogenic composition according to claim 264, wherein the carrier is a polypeptide from *Mycobacterium tuberculosis* (BCG).

272. The immunogenic composition according to claim 265, wherein the bacterial toxoid is tetanus toxoid.

273. The immunogenic composition according to claim 265, wherein the bacterial toxoid is CRM<sub>197</sub>.

274. The immunogenic composition according to claim 264, wherein the carrier is Streptococcal rC5a peptidase.

275. The immunogenic composition according to claim 264, wherein the carrier is *Streptococcus pyogenes* ORF1224.

276. The immunogenic composition according to claim 264, wherein the carrier is *Streptococcus pyogenes* ORF1664.

277. The immunogenic composition according to claim 264, wherein the carrier is *Streptococcus pyogenes* ORF2452.

278. The immunogenic composition according to claim 264, wherein the carrier is *Chlamydia pneumoniae* ORF T367.

279. The immunogenic composition according to claim 264, wherein the carrier is *Chlamydia pneumoniae* ORF T858.

280. The immunogenic composition according to claim 262, wherein the carrier is a growth factor or a hormone, which stimulates or enhances immune response.

281. The immunogenic composition according to claim 280, wherein the growth factor or hormone is selected from a group consisting of IL-1, IL-2,  $\gamma$ -interferon, IL-10, GM-CSF, MIP-1 $\alpha$ , MIP-1 $\beta$ , and RANTES.

282. The immunogenic composition according to claim 262, wherein the peptide immunogen is selected from the group consisting of a bacterial protein, a viral protein, a fungal protein, a parasite protein, and a eukaryotic protein.

283. The immunogenic composition according to claim 282, wherein the peptide immunogen is derived from a protein antigen from a bacterium.

284. The immunogenic composition according to claim 283, wherein the bacterium is selected from the group consisting of *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Neisseria meningitidis*, *Neisseria gonorrhoeae*, *Haemophilus influenzae*, *Escherichia coli*, *Klebsiella enterobacter*, *Listeria monocytogenes*, *Vibrio cholerae*, *Clostridium perfringens*, *Clostridium botulinum*, *Pseudomonas* species, *Salmonella typhimurium*, *Borrelia burgdorferi*, *Shigella flexneri*, *Shigella boydii*, *Shigella dysenteriae*, *Alloiococcus otitidis* and Group B streptococci.

285. The immunogenic composition according to claim 282, wherein the peptide immunogen is derived from a protein antigen from a virus.

286. The immunogenic composition according to claim 285, wherein the virus is selected from the group consisting of a human immunodeficiency virus (HIV), a herpes simplex virus (HSV), a human papilloma virus (HPV), a parainfluenza virus (PIV), a vesicular stomatitis virus (VSV), a respiratory syncytial virus (RSV), an Epstein-Barr virus (EBV), a coronavirus, a vaccinia virus, a rotavirus, a rabies virus, a hepatitis C virus (HCV) and a hepatitis B virus (HBV).

287. The immunogenic composition according to claim 282, wherein the peptide immunogen is derived from a protein antigen from a fungus.



288. The immunogenic composition according to claim 287, wherein the fungus is selected from the group consisting of *Candida albicans*, *Cryptococcus neoformans*, *Coccidioides*, *Histoplasma*, and *Aspergillus*.

289. The immunogenic composition according to claim 282, wherein the peptide immunogen is derived from a protein antigen from a parasite.

290. The immunogenic composition according to claim 289, wherein the parasite is selected from the group consisting of a *Plasmodium*, a *Trypanosome*, a *Schistosoma*, and a *Leishmania*.

291. The immunogenic composition according to claim 282, wherein the peptide immunogen is derived from a protein antigen from a eukaryote.

292. The immunogenic composition according to claim 291, wherein the eukaryote is a human.

293. The immunogenic composition according to claim 292, wherein peptide immunogen from a human is derived from a malignant tumor.

294. The immunogenic composition according to claim 293, wherein the peptide immunogen is selected from the group consisting of a renal cell carcinoma antigen, a breast carcinoma antigen, a carcinoembryonic antigen, a melanoma antigen, and a prostate cancer specific antigen.

295. The immunogenic composition according to claim 292, wherein the peptide immunogen is from a human A $\beta$  polypeptide.

296. The immunogenic composition according to claim 295, wherein the peptide immunogen is derived from the N-terminal region of A $\beta$  polypeptide.

297. The immunogenic composition according to claim 295, wherein the peptide immunogen is derived from the C-terminal region of A $\beta$  polypeptide.

298. The immunogenic composition according to claim 295, wherein the peptide immunogen is derived from the internal region of A $\beta$  polypeptide.

299. The immunogenic composition according to claim 295, wherein the A $\beta$  peptide immunogen is derived from the N-terminal region of A $\beta$  polypeptide, and is a fragment of A $\beta$  selected from the group consisting of A $\beta$ 1-5, 1-6, 1-7, 1-10, 1-12, 3-7, 1-3, and 1-4.

300. The immunogenic composition according to claim 295, wherein the A $\beta$  peptide immunogen is a fragment of A $\beta$  selected from the group consisting of A $\beta$  7-11, 3-28, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 17-28, 1-28, 25-35, 35-40 and 35-42.

301. The immunogenic composition according to claim 295, wherein one molecule of an A $\beta$  peptide immunogen is fused at its C-terminus to the N-terminus of another molecule of the same A $\beta$  peptide immunogen.

302. The immunogenic composition according to claim 295, wherein one molecule of an A $\beta$  peptide immunogen is fused at its C-terminus to the C-terminus of another molecule of the same A $\beta$  peptide immunogen.

303. The immunogenic composition according to claim 295, wherein one molecule of an A $\beta$  peptide immunogen is fused at its C-terminus to the C-terminus of a molecule of a different A $\beta$  peptide immunogen.

304. The immunogenic composition according to claim 295, wherein one molecule of an A $\beta$  peptide immunogen is fused at its N-terminus to the C-terminus of a molecule of a different A $\beta$  peptide immunogen.

305. The immunogenic composition according to claim 301, 302, 303, or 304, wherein the A $\beta$  fragment is derived from the N-terminal region of A $\beta$  polypeptide and is selected from the group consisting of A $\beta$ 1-5, 1-6, 1-7, 1-10, 1-12, 3-7, 1-3, and 1-4.

306. The immunogenic composition according to claim 301, 302, 303, or 304, wherein the A $\beta$  fragment is a fragment of A $\beta$  selected from the group consisting of A $\beta$  7-11, 3-28, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 17-28, 1-28, 25-35, 35-40 and 35-42.

307. The immunogenic composition according to claim 295, wherein one or more molecules of an A $\beta$  peptide immunogen are linked to one or more molecules of a heterologous peptide.

308. The immunogenic composition according to claim 307, wherein the A $\beta$  peptide immunogen is derived from the N-terminal region of A $\beta$  polypeptide, and is selected from the group consisting of A $\beta$ 1-5, 1-6, 1-7, 1-10, 1-12, 3-7, 1-3, and 1-4.

309. The immunogenic composition according to claim 307, wherein the A $\beta$  peptide immunogen is a fragment of A $\beta$  selected from the group consisting of A $\beta$  7-11, 3-28, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 17-28, 1-28, 25-35, 35-40 and 35-42.

310. The immunogenic composition according to claim 295, wherein one or more molecules of an A $\beta$  peptide immunogen are linked together in a multiple antigenic peptide (MAP) configuration.

311. The immunogenic composition according to claim 295, wherein one or more molecules of an A $\beta$  peptide immunogen are linked with one or more molecules of a different A $\beta$  peptide immunogen in a multiple antigenic peptide (MAP) configuration.

312. The immunogenic composition according to claim 310 or 311, wherein the A $\beta$  peptide immunogen is derived from the N-terminal region of A $\beta$  polypeptide, and is selected from the group consisting of A $\beta$ 1-5, 1-6, 1-7, 1-10, 1-12, 3-7, 1-3, and 1-4.

313. The immunogenic composition according to claim 310 or 311, wherein the A $\beta$  peptide immunogen is a fragment of A $\beta$  selected from the group consisting of A $\beta$  7-11, 3-28, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 17-28, 1-28, 25-35, 35-40 and 35-42.

314. The immunogenic composition according to claim 262, wherein one or more adjuvants are selected from the group consisting of GM-CSF, 529 SE, IL-12, aluminum phosphate, aluminum hydroxide, *Mycobacterium tuberculosis*, *Bordetella pertussis*, bacterial lipopolysaccharides, aminoalkyl glucosamine phosphate compounds, MPL™ (3-O-deacylated monophosphoryl lipid A), a polypeptide, Quil A, STIMULON™ QS-21, a pertussis toxin (PT), an *E.coli* heat-labile toxin (LT), IL-1  $\alpha$ , IL-1  $\beta$ , IL-2, IL-4, IL-5, IL-6,

IL-7, IL-8, IL-10, IL-13, IL-14, IL-15, IL-16, IL-17, IL-18, interferon- $\alpha$ , interferon- $\beta$ , interferon- $\gamma$ , G-CSF, TNF- $\alpha$  and TNF- $\beta$ .

315. The immunogenic composition of claim 314, wherein the peptide immunogen is A $\beta$ , the carrier is CRM<sub>197</sub>, and the adjuvant is 529 SE.

316. A method for inducing an immune response in a mammalian subject, which comprises administering an effective amount of the immunogenic composition of claim 262 to the subject.

317. The method according to claim 316, wherein the carrier is selected from the group consisting of human serum albumin, keyhole limpet hemocyanin (KLH), immunoglobulin molecules, thyroglobulin, ovalbumin, influenza hemagglutinin, PADRE polypeptide, malaria circumsporozoite (CS) protein, hepatitis B surface antigen (HBsAg<sub>19-28</sub>), Heat Shock Protein (HSP) 65, *Mycobacterium tuberculosis*, cholera toxin, cholera toxin mutants with reduced toxicity, diphtheria toxin, CRM<sub>197</sub> protein that is cross-reactive with diphtheria toxin, recombinant Streptococcal C5a peptidase, *Streptococcus pyogenes* ORF1224, *Streptococcus pyogenes* ORF1664, *Streptococcus pyogenes* ORF2452, *Chlamydia pneumoniae* ORF T367, *Chlamydia pneumoniae* ORF T858, Tetanus toxoid, HIV gp120 T1, components recognizing microbial surface adhesive matrix molecules (MSCRAMMS), growth factors, hormones, cytokines and chemokines.

318. The method according to claim 316, wherein the carrier contains a T-cell epitope.

319. The method according to claim 318, wherein the carrier is a bacterial toxoid.

320. The method according to claim 318, wherein the carrier is influenza hemagglutinin.

321. The method according to claim 318, wherein the carrier is PADRE polypeptide.

322. The method according to claim 318, wherein the carrier is malaria circumsporozoite (CS) protein.

323. The method according to claim 318, wherein the carrier is Hepatitis B surface antigen.
324. The method according to claim 318, wherein the carrier is heat shock protein 65 (HSP 65).
325. The method according to claim 318, wherein the carrier is a polypeptide from *Mycobacterium tuberculosis* (BCG).
326. The method according to claim 319, wherein the bacterial toxoid is tetanus toxoid.
327. The method according to claim 319, wherein the bacterial toxoid is CRM<sub>197</sub>.
328. The method according to claim 318, wherein the carrier is Streptococcal rC5a peptidase.
329. The method according to claim 318, wherein the carrier is *Streptococcus pyogenes* ORF1224.
330. The method according to claim 318, wherein the carrier is *Streptococcus pyogenes* ORF1664.
331. The method according to claim 318, wherein the carrier is *Streptococcus pyogenes* ORF2452.
332. The method according to claim 318, wherein the carrier is *Chlamydia pneumoniae* ORF T367.
333. The method according to claim 318, wherein the carrier is *Chlamydia pneumoniae* ORF T858.
334. The method according to claim 316, wherein the carrier is a growth factor or hormone, which stimulates or enhances immune response.

335. The method according to claim 334, wherein the growth factor or hormone is selected from a group consisting of IL-1, IL-2,  $\gamma$ -interferon, IL-10, GM-CSF, MIP-1 $\alpha$ , MIP-1 $\beta$ , and RANTES.

336. The method according to claim 316, wherein the peptide immunogen is selected from the group consisting of a bacterial protein, a viral protein, and a eukaryotic protein.

337. The method according to claim 336, wherein the peptide immunogen is derived from a protein antigen from a bacterium.

338. The method according to claim 337, wherein the bacterium is selected from *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Neisseria meningitidis*, *Neisseria gonorrhoeae*, *Haemophilus influenzae*, *Escherichia coli*, *Klebsiella enterobacter*, *Listeria monocytogenes*, *Vibrio cholerae*, *Clostridium perfringens*, *Clostridium botulinum*, *Pseudomonas* species, *Salmonella typhimurium*, *Borrelia burgdorferi*, *Shigella flexneri*, *Shigella boydii*, *Shigella dysenteriae*, *Alloiococcus otitidis* and Group B streptococci.

339. The method according to claim 336, wherein the peptide immunogen is derived from a protein antigen from a virus.

340. The method according to claim 339, wherein the virus is selected from the group consisting of a human immunodeficiency virus (HIV), a herpes simplex virus (HSV), a human papilloma virus (HPV), a parainfluenza virus (PIV), a vesicular stomatitis virus (VSV), a respiratory syncytial virus (RSV), a Epstein-Barr virus (EBV), a coronavirus, a vaccinia virus, a rotavirus, a rabies virus, a hepatitis C virus (HCV) and a hepatitis B virus (HBV).

341. The method according to claim 336, wherein the peptide immunogen is derived from a protein antigen from a fungus.

342. The method according to claim 341, wherein the fungus is selected from the group consisting of a *Candida* species, a *Cryptococcus* species, a *Coccidioides* species, a *Histoplasma* species, and an *Aspergillus* species.

343. The method according to claim 336, wherein the peptide immunogen is derived from a protein antigen from a parasite.

344. The method according to claim 343, wherein the parasite is selected from the group consisting of a Plasmodium, a Trypanosome, a Schistosoma, and a Leishmania.

345. The method according to claim 336, wherein the peptide immunogen is derived from a protein antigen from a eukaryote.

346. The method according to claim 345, wherein the eukaryote is a human.

347. The method according to claim 347, wherein peptide immunogen from a human is derived from a malignant tumor.

348. The method according to claim 347, wherein the peptide immunogen is derived from a renal cell carcinoma antigen, a breast carcinoma antigen, a carcinoembryonic antigen, a melanoma (MAGE-1) antigen, and a prostate cancer specific antigen.

349. The method according to claim 346, wherein the peptide immunogen is from a human A $\beta$  polypeptide.

350. The method according to claim 349, wherein the peptide immunogen is derived from the N-terminal region of A $\beta$  polypeptide.

351. The method according to claim 349, wherein the peptide immunogen is derived from the C-terminal region of A $\beta$  polypeptide.

352. The method according to claim 349, wherein the peptide immunogen is derived from the internal region of A $\beta$  polypeptide.

353. The method according to claim 350, wherein the A $\beta$  peptide immunogen is derived from the N-terminal region of A $\beta$  polypeptide, and is a fragment of A $\beta$  selected from the group consisting of A $\beta$ 1-5, 1-6, 1-7, 1-10, 1-12, 3-7, 1-3, and 1-4.

354. The method according to claim 349, wherein the A $\beta$  peptide immunogen is a fragment of A $\beta$  selected from the group consisting of A $\beta$  7-11, 3-28, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 17-28, 1-28, 25-35, 35-40 and 35-42.

355. The method according to claim 349, wherein one molecule of an A $\beta$  peptide immunogen is fused at its C-terminus to the N-terminus of another molecule of the same A $\beta$  peptide immunogen.

356. The method according to claim 349, wherein one molecule of an A $\beta$  peptide immunogen is fused at its C-terminus to the C-terminus of another molecule of the same A $\beta$  peptide immunogen.

357. The method according to claim 349, wherein one molecule of an A $\beta$  peptide immunogen is fused at its C-terminus to the C-terminus of a molecule of a different A $\beta$  peptide immunogen.

358. The method according to claim 349, wherein one molecule of an A $\beta$  peptide immunogen is fused at its N-terminus to the C-terminus of a molecule of a different A $\beta$  peptide immunogen.

359. The method according to claim 355, 356, 357, or 358, wherein the A $\beta$  peptide immunogen is derived from the N-terminal region of A $\beta$  polypeptide, and is selected from the group consisting of A $\beta$ 1-5, 1-6, 1-7, 1-10, 1-12, 3-7, 1-3, and 1-4.

360. The method according to claim 355, 356, 357, or 358, wherein the A $\beta$  peptide immunogen is a fragment of A $\beta$  selected from the group consisting of A $\beta$  7-11, 3-28, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 17-28, 1-28, 25-35, 35-40 and 35-42.

361. The method according to claim 349, wherein one or more molecules of an A $\beta$  peptide immunogen are linked to one or more copies of a heterologous peptide.

362. The method according to claim 361, wherein the A $\beta$  peptide immunogen is derived from the N-terminal region of A $\beta$  polypeptide, and is selected from the group consisting of A $\beta$ 1-5, 1-6, 1-7, 1-10, 1-12, 3-7, 1-3, and 1-4.



363. The method according to claim 361, wherein the A $\beta$  peptide immunogen is selected from the group consisting of A $\beta$  7-11, 3-28, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 17-28, 1-28, 25-35, 35-40 and 35-42.

364. The method according to claim 349, wherein one or more molecules of an A $\beta$  peptide immunogen are linked together in a multiple antigenic peptide (MAP) configuration.

365. The method according to claim 349, wherein one or more molecules of an A $\beta$  peptide immunogen are linked with one or more molecules of a different A $\beta$  peptide immunogen in a multiple antigenic peptide (MAP) configuration.

366. The method according to claim 364 or 365, wherein the A $\beta$  peptide immunogen is derived from the N-terminal region of A $\beta$  polypeptide, and is a fragment of A $\beta$  selected from the group consisting of A $\beta$ 1-5, 1-6, 1-7, 1-10, 1-12, 3-7, 1-3, and 1-4.

367. The method according to claim 364 or 365, wherein the A $\beta$  peptide immunogen is a fragment of A $\beta$  selected from the group consisting of A $\beta$  7-11, 3-28, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 17-28, 1-28, 25-35, 35-40 and 35-42.

368. The method according to claim 262, wherein one or more adjuvants are selected from the group consisting of GM-CSF, 529 SE, IL-12, aluminum phosphate, aluminum hydroxide, *Mycobacterium tuberculosis*, *Bordetella pertussis*, bacterial lipopolysaccharides, aminoalkyl glucosamine phosphate compounds, MPL™ (3-O-deacylated monophosphoryl lipid A), a polypeptide, Quil A, STIMULON™ QS-21, a pertussis toxin (PT), an *E. coli* heat-labile toxin (LT), IL-1  $\alpha$ , IL-1  $\beta$ , IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-13, IL-14, IL-15, IL-16, IL-17, IL-18, interferon- $\alpha$ , interferon- $\beta$ , interferon- $\gamma$ , G-CSF, TNF- $\alpha$  and TNF- $\beta$ .

369. The method according to claim 368, wherein the peptide immunogen is A $\beta$ , the carrier is CRM<sub>197</sub>, and the adjuvant is 529 SE.